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NREM and REM Sleep Parasomnias: Clinical Cases and Literature Review

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Summary. Parasomnias are a group of sleep disorders that manifest as abnormal behaviour or movements while falling asleep, during sleep, or before awakening. According to the International Classification of Sleep Disorders (ICSD-3), parasomnias are subdivided into non-rapid eye movement (NREM) and rapid eye movement (REM) parasomnias. Main types of NREM parasomnias include disorders of arousal which consist of confusional arousals, sleepwalking, and sleep terrors, as well as sleep-related abnormal sexual behaviour and sleep-related eating disorder (SRED). The prevalence of NREM parasomnias in children and adolescents is higher than in adults. NREM parasomnias are often benign, self-limited, or resolved with non-pharmacological treatment, while REM sleep behaviour disorder (example of REM parasomnias) is much more likely to occur in adult age and is associated with neurodegenerative diseases. There are 3 types of parasomnias associated with REM sleep: REM sleep behaviour disorder (RBD), isolated sleep paralysis, and nightmare disorder. Parasomnias can significantly disrupt the sleep quality of patients and their bed partners, daytime wakefulness, and can be hazardous. Detailed sleep history and clinical examination are of essential significance in differential diagnosis between sleep disorders, nocturnal epilepsy, and psychiatric disorders. Non-pharmacological interventions such as sleep hygiene and safe sleeping environment play an important role in management of parasomnias.

Keywords: sleep disorders, NREM parasomnias, REM parasomnias, polysomnography.

INTRODUCTION

Parasomnias are a group of sleep disorders that manifest as abnormal behaviour or movements while falling asleep, during sleep, or before awakening. There are 3 polysomnographic sleep stages: transitional stage between wakefulness and sleep, non-rapid eye movement (NREM) sleep, and rapid eye movement (REM) sleep, which change cyclically. NREM sleep is subdivided into three stages: N1 stage manifesting as drowsy, transitional state between wakefulness and sleep; N2 stage which comprises the largest part of the NREM sleep; and N3 stage, or deep sleep stage, during which the threshold of arousal is higher thus stronger stimuli are needed to provoke awakening. According to the International Classification of Sleep Disorders (ICSD-3), parasomnias are subdivided into NREM parasomnias and REM parasomnias [1].

PREVALENCE AND PATHOGENESIS

Main types of NREM parasomnias include disorders of arousal which consist of confusional arousals, sleepwalking, sleep terrors, as well sleep-related abnormal sexual behaviour and sleep-related eating disorder (SRED). NREM parasomnias typically occur during N3, less frequently during N2 stage, whereas in parasomnia overlap disorder, abnormal behaviours can arise from both NREM and REM sleep. NREM parasomnias can manifest at any age, although commonly they occur in childhood and adolescence. As a result, the prevalence of sleepwalking in children is 14.5% [2], while only 1.7% of adults experience sleepwalking [3].

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Although pathophysiology of NREM parasomnias is not completely understood, predisposing, priming, and precipitating factors of NREM parasomnias have been identified. In cases where predisposing, priming, and precipitating factors combine simultaneously, this leads to the occurrence of abnormal and unwanted sleep behaviour. Predisposing factors mainly include genetics and family history of abnormal sleep behaviours. As estimated in a large prospective longitudinal cohort study in Quebec in 1997, the likelihood of a child manifesting NREM behaviours is 22% regardless of family history, whereas prevalence of 45% is estimated if either of parents have the disorder. Accordingly, if both parents experience NREM sleep disorder, the likelihood of its manifestation in the subsequent generation is 60% [4].

Recently conducted retrospective study has determined significance of HLA DQB1*05:01 allele in the inheritance of NREM parasomnias. There is a statistically significant difference of HLA DQB1*05:01 allele incidence rates between healthy participants and patients with NREM parasomnia [5]. It is important to clarify, though, that genetics only increase the susceptibility to NREM sleep disorder. Priming factors include conditions and medications that facilitate partial awakening as they lengthen the duration of NREM sleep stage, increase the threshold of arousal, or fragmentate sleep. These include sleep deprivation, circadian sleep-wake rhythm disorders, shift work, particular medications (Z-drugs, lithium, some antidepressants, anticholinergic drugs), alcohol consumption, stress, hyperthyroidism, migraine, past head injury, encephalitis, stroke, and neurodegenerative diseases [4]. Precipitating factors cause partial awakening, which manifests as particular NREM parasomnia phenotype. These factors can be subdivided into external stimuli such as noise, external physical stimuli, and contact with a sleeping partner, and internal stimuli such as other sleep disorders.

For patients with NREM parasomnias, the first-line intervention is to provide advice on safety, sleep hygiene, and management of priming and precipitating factors. NREM parasomnias in children are usually benign, transient, self-limited, or can be resolved with proper sleep hygiene [6]. Although, they can persist into adulthood or occur *de novo* in adult age [4]. It has been determined that adult patients with NREM parasomnias are 2 times more likely to have neurological comorbidities [7]. Furthermore, NREM parasomnias that appeared in childhood and persisted into adulthood present with more complex and dangerous behaviours than those that occurred *de novo* [8].

There are 3 types of parasomnias associated with the REM sleep: REM sleep behaviour disorder, isolated sleep paralysis, and nightmare disorder. Prevalence of the nightmare disorder and isolated sleep paralysis is higher in younger patients, whereas REM sleep behaviour disorder occurs more frequently in adult male patients older than 50 years with the incidence rate of 0.38–0.5% [9]. Although there is convincing evidence that incidence rate is even higher in patients older than 70 who present with comorbid neurodegenerative diseases. REM sleep behaviour disorder can be the first symptom of neurodegenerative diseases, especially -synocleinopathies, such as Parkinson's disease, Lewy body dementia, or multiple system atrophy. It is estimated that 90% of patients, who are diagnosed with idiopathic REM sleep behaviour disorder, few years and even decades later are diagnosed with neurodegenerative disease [10].

Prognosis of REM sleep parasomnias is less established for female and pediatric patients. REM sleep parasomnias are associated with narcolepsy, periodic limb movements, neurological and autoimmune diseases, and consumption of or withdrawal from SSRI antidepressants in pediatric and adolescent population [10]. Related neurological diseases are spinocerebellar ataxia, stroke, brain tumours, multiple sclerosis, Guillain-Barre syndrome, and limbic encephalitis. Discontinuation of paroxetine, fluoxetine, venlafaxine, mirtazapine, and barbiturates is also related to abnormal behaviours during REM sleep. In addition, continuous positive airway pressure therapy and alcohol withdrawal can facilitate rebound REM sleep parasomnias [11]. Abnormal sleep behaviours in older age are associated with sleep-related traumas; even 32–65% of patients with REM sleep behaviour disorder experience traumas or harm their family member or sleeping partners during sleep [9].

CLINICAL FEATURES

Disorders of arousal (DOAs) are divided into several subtypes: confusional arousals, sleepwalking, and sleep terrors. It is believed that these subtypes are different phenotypes caused by the same pathophysiological mechanism rather than separate and independent clinical conditions. This hypothesis is backed up by the fact that patients quite often experience episodes of various NREM parasomnias, even if one of them is dominant [4, 6]. NREM parasomnias are considered to be an in-between state of wakefulness and NREM sleep, therefore they present with characteristic elements of both of these physiological conditions. Individuals may have their eyes open, engage in complex activities, and maintain a verbal contact with other people. On the other hand, patients usually do not remember the episode or can recall only a few vague visual or auditory details. In addition, disorientation in time and space as well as altered perception of the environment and decreased response to the stimuli can be observed [6, 12]. According to some research data, NREM parasomnias may be a result of altered neural networks. In this case, sleep and wakefulness may not be a global whole brain process, and different regions of the brain can be in incompatible states presenting as a clinical condition that shows characteristics of both arousal and sleep [6, 12].

During an episode of confusional arousal, an individual sits up in bed, may look around and appear confused. This behaviour is often accompanied by sleep talking which presents with slow slurred speech and blunt re-

sponses to questions [6]. If the patient tries to get up and get out of bed, confusional arousal can turn into somnambulism. Nonetheless, sleepwalking may start suddenly when the patient jumps out of bed. Sleepwalkers often wander around the bedroom aimlessly with their eyes open or appear to be searching for something. More complex behaviours are not uncommon as well – patients may move furniture, climb on a chair to change a lightbulb, play an instrument, or even try to drive [4, 11]. Several cases of dangerous behaviours have been described in the literature. One of these case reports describes a parasomnia episode in which a 28-year-old male attempted to strangulate himself [13]. In another case, a 10-year-old girl fell out of a window while sleep walking [14]. Lastly, sleep terrors are described as sudden episodes of intense fear, during which an individual looks frightened, may sit up in bed, and scream or cry. This behaviour is followed by intense autonomic reactions, such as tachycardia, tachypnoea, mydriasis, increased muscle tone, and perspiration [4, 6].

Sleep related eating disorders and sleep related sexual behaviours are distinguished as separate types of NREM parasomnias. SRED manifests as recurring and involuntary episodes of eating or drinking that occur during the state of incomplete awakening from sleep. Eating not only ordinary meals, often high in calories, but bizarre and inedible products such as raw meat, pet food, and cigarettes or cleaning agents, is common [11]. A hazard to one's health is not only the choice of food and beverages, but also handling of knives and other dangerous kitchen items. Meanwhile, sleep related sexual behaviours usually present as various vocalisations, masturbation, or an attempt to initiate a sexual intercourse [4].

These sleep disturbances are known to affect the normal structure of NREM sleep, however, there is a lack of data on how NREM parasomnias disturb patients' everyday life. According to the data of several studies, around 40% of patients suffering from disorders of arousal have excessive daytime sleepiness. In addition, one large scale case-control study has found that DOA patients complain of increased cognitive fatigue, mostly affecting visuospatial working memory and selective visual attention [6].

REM sleep parasomnias group consists of REM sleep behaviour disorder, recurrent isolated sleep paralysis, and nightmare disorder. Individuals who are suffering from REM sleep behaviour disorder experience episodes of dream enactment, which can occur at various frequency, from several times per year to every night. The content of these dreams, as a rule, is intense, action-filled, and full of unpleasant imagery, for example, the patient might be pursued and attacked by hazardous animals or people [10]. Subsequently, patients shout, gesticulate or attempt to punch, kick, or run away from the attacker. Such intense dream enactment can lead to minor injuries: subcutaneous hematomas, scratches, or wounds. Scientific literature also describes more severe cases of injuries, such as bone fractures or subdural hematomas [15, 16]. Self-harm has also been reported, for example, a case of a 55-year-old male who bit off his index finger to the tendon and had to undergo surgery to repair the tendon [13]. Furthermore, a possibility of injuring one's bed partner also exists. In addition to aggressive behaviours, REM sleep behaviour disorder can also manifest as non-aggressive actions such as laughing or singing, imitating dance movements, or imaginary cigarette smoking [9]. This disorder quite often is the first sign of neurodegenerative disease, especially -synocleinopathy. The risk to be diagnosed with neurodegenerative disease is increased if other prodrome symptoms are present, such as subjective complaints or asymptomatic decline in cognitive abilities, subtle motor deficits, hyposmia, constipation or orthostatic hypotension [17]. Secondary REM sleep behaviour disorder, caused by the damage of brainstem centres responsible for muscle atonia, is also distinguished. In most cases, the impairment of the mentioned brain areas is a consequence of multiple sclerosis, vascular disorders, or brainstem tumour growth [10].

Isolated recurrent sleep paralysis is diagnosed when episodes of sleep paralysis keep repeating and no signs of narcolepsy or other sleep disorder are observed. Usually caused by sleep deprivation, the condition is a result of REM sleep muscle atonia perseverating into wakefulness. In addition to complete or partial inability to move, most patients also experience vivid and unpleasant dreams. Visual, auditory, or tactile hallucinations may also be present, thus an individual feels the urge to escape from a threatening situation. Due to loss of muscle tone patients may feel trapped and unable to flee, and episodes of sleep paralysis can be frightening and severely distressing [18]. Nightmare disorder is characterized as recurrent highly dysphoric dreams that cause distress and clinically significant mood disturbances, as well as social or cognitive impairment. Such nightmares are often a part of post-traumatic stress disorder or other psychiatric comorbidity [19].

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

For most types of parasomnias, the diagnosis can be made based on anamnestic data, thus accurate and detailed collection of medical history is one of the first and most important steps of the diagnostic process. Most patients do not remember the episodes of NREM parasomnias, and interviewing witnesses of such occurrences, especially the patient's bed partner, is required. In addition, it may also be advisable to take videos of the patient during an episode of parasomnia. Taking a medical history from the bed partner is also helpful in cases of REM sleep behaviour disorder since nearly half of the patients cannot recall the content of their dreams, do not know that they have episodes of sleep disturbance, or are unable to describe them in detail because of cognitive impairment [9].

Family history of sleep disorders, as well as identification of comorbidities and medications that exacerbate the disease, should also be a part of the diagnostic process. For example, individuals treated with antidepressants have 5-fold increased risk of developing REM sleep behaviour

Table 1. **Diagnostic criteria for REM sleep without atonia (RSWA)** (adapted from [23])

AASM (American Academy of Sleep Medicine) Manual for the Scoring of Sleep and Associated Events RSWA criteria	
Muscles monitored by EMG	Chin, *m. tibialis anterior*
RSWA criteria	Tonic RSWA: chin amplitude higher than the minimal amplitude in NREM sleep for 50% of 30-second epoch Phasic RSWA: transient muscle activity lasting 0.1–5 seconds and with amplitude 4 times the background EMG in 5 of 3-second mini-epochs within a 30-second epoch
SINBAR (Sleep Innsbruck Barcelona) RSWA criteria	
Muscles monitored by EMG	Chin, *m. flexor digitorum superficialis*
RSWA criteria	Tonic RSWA: chin amplitude twice the background EMG or 10mV for 50% of 30-second epoch (measured in chin EMG) Phasic RSWA: transient muscle activity lasting 0.1–5 seconds and with amplitude twice the background EMG (or twice the tonic amplitude when superimposed on tonic activity) in 3-second mini-epoch (measured in chin and *m. flexor digitorum superficialis* EMG) Any RSWA: either tonic activity, phasic activity, or a combination of both in 3-second mini-epoch (measured in chin EMG) Cut-off for RBD: any activity in 27% of REM 30-second epochs/any activity in 32% of REM 3-second mini-epochs
Montreal RSWA criteria	
Muscles monitored by EMG	Chin
RSWA criteria	Tonic RSWA: chin amplitude twice the background EMG or 10mV for 50% of 20-second epoch Phasic RSWA: transient muscle activity lasting 0.1–10 seconds and 4 times the amplitude of background amplitude in 2 second mini-epochs Cut-off for RBD: tonic activity in 30% of the REM epochs/phasic activity in 15% of the mini-epochs
McCarter and coworkers RSWA criteria	
Muscles monitored by EMG	Chin, *m. tibialis anterior*
RSWA criteria	Tonic RSWA: chin amplitude twice the background EMG or 10mV for 50% (measured in chin and *m. tibialis anterior* EMG) Phasic RSWA: – transient muscle activity lasting 0.1–14.9 seconds and with amplitude 4 times the background EMG (or twice the tonic EMG when superimposed) in 5 of 3 second mini-epochs within epoch (measured in chin and *m. tibialis anterior* EMG) – each phasic muscle burst during REM sleep is measured directly for each muscle, resulting in an average phasic muscle burst duration Any RSWA: either tonic activity, phasic activity, or a combination of both (5–15 seconds) in 3-second mini-epoch (measured in chin and *m. tibialis anterior* EMG) Any activity in 43.4% of 3 second-mini epochs/chin phasic muscle burst duration of 0.65 seconds/AT phasic muscle burst duration of 0.79 seconds
Bliwise and coworkers RSWA criteria	
Muscles monitored by EMG	Chin, *m. tibialis anterior*, *m. brachioradialis*
RSWA criteria	Phasic activity/phasic EMG metric (PEM): bursts of EMG activity 100 milliseconds, with an amplitude 4 times the background EMG in the pre-sleep baseline. PEMs were scored in 2.5-second mini-epochs

disorder. Moreover, probability of developing such a disorder in people with established psychiatric comorbidity is 10 times higher [17]. Thus, these data are extremely valuable in identifying predisposing factors and making recommendations for lifestyle modification. The possibility of additional sleep disorders should be evaluated since such conditions can precipitate episodes of parasomnias. Microarousals caused by respiratory events such as apneas or hypopneas and excessive movements such as periodic limb movements are known to provoke episodes of NREM parasomnias [4]. Physicians should be aware of parasomnia overlap disorder defined by ICSD-3 as a condition presenting with features of REM sleep behaviour disorder, as well as symptoms of arousal disorder, sleep related eating disorder, sexsomnia, or rhythmic movement disorder. For example, patients with Parkinson's disease can experience both RBD and NREM parasomnias [20]. Thus, if a specific parasomnia is suspected, other possible parasomnias should be evaluated.

The role of polysomnography in the diagnostic process of parasomnias is debatable. The test is not necessary for the diagnosis of NREM parasomnia, nonetheless it is quite often used to rule out concomitant sleep disorders such as overlapping parasomnia disorder, sleep apnea, or periodic limb movement disorder. Sleep study is also helpful when differentiating between parasomnias and nocturnal frontal

Table 2. **Characteristics of sleep events** [9, 10, 24, 25]

	Disorders of arousal	**Sleep related eating disorder**	**REM sleep behaviour disorder**	**Nightmare disorder**	**Recurrent isolated sleep paralysis**	**Nocturnal seizures**	**Psychiatric disorders (panic attacks, PTSD)**
Timing	First third to first half of the night, usually during N3 stage	First third to first half of the night	During REM sleep, latter half of the night sleep period	During REM sleep, latter half of the night sleep period	Before awakening	Sporadic, more common during N2 stage	Sporadic
Eye opening	+	+	–	–	+	–	+
Event memory	Partial (few fragments) or none	Partial or none	Detailed dream recall	Yes	Yes	Various	Various
Duration	Minutes	Minutes	Seconds to minutes	Movements last for a few seconds	Seconds to minutes	Minutes	Minutes to Hours
Polysomnography findings	Arousal from slow wave sleep, usually during N3 stage	Arousal from slow wave sleep	REM sleep without atonia	Arousal from REM sleep	Arousal from REM sleep	Epileptic activity more common in NREM sleep, uncommon in REM sleep	Wake state

lobe epilepsy or complex focal seizures [4]. Disorders of arousal present with typical polysomnographic features such as uncompromised sleep architecture, but with increased number of awakenings, arousals, or microarousals from slow wave sleep (N3 stage) [6]. Some parasomnia episodes are not clinically present, and during slow wave sleep only occurrences of increased spontaneous awakening and arousal can be seen on EEG. Reports in the scientific literature also describe observations of increased cyclic alternating pattern rate and hypersynchronous delta waves, defined as continuous high-voltage (>150 μV) delta waves occurring during slow wave sleep in cases of NREM parasomnias [21]. Similarly, polysomnography is not required for suspected nightmare disorder or isolated recurrent sleep paralysis, yet it is recommended for differentiating them from narcolepsy or REM sleep behaviour disorder [19].

To conclude about the importance of polysomnography in the diagnostic process of parasomnias, it is recommended in cases of atypical history or course of disease, if the patient experiences excessive daytime sleepiness, stereotypical behaviours, when other sleep disorders are suspected, or when the patient is at risk of hurting himself or others around him [22].

An exception is REM sleep behaviour disorder, which can be suspected based on the medical history of the patient and his relatives, however, to make an accurate diagnosis video polysomnography is necessary. A typical feature of REM sleep behaviour disorder observed on polysomnography is REM sleep without atonia, which can manifest as either as phasic twitch activity or/and excess of muscle tone during REM sleep [9, 17]. It can be challenging to identify the REM sleep stage in the absence of muscle atonia, therefore it is customary to distinguish between REM stage based on EEG and electrooculography data. Sleep Innsbruck Barcelona (SINBAR) group assessed the electromyography data of various limb muscle groups and noticed that excessive muscle activity is present not only in traditionally evaluated *m. mentalis*, but in such limb muscles as *m. flexor digitorum superficialis*. Although recommended, *m. flexor digitorum superficialis* is not commonly seen on routine video polysomnographic tests [9]. Current REM sleep without diagnostic criteria for atonia are presented in Table 1 [23].

Previously mentioned ICSD-3, DSM-5, and ICD-10 classification systems also describe diagnostic criteria for parasomnias. But, despite this, a number of diagnostic difficulties arise due to inconsistencies in the diagnostic criteria presented by these systems. Currently, ICSD-3 diagnostic criteria are most commonly used by sleep medicine specialists [4].

A large part of the diagnostic challenge is differential diagnostics between different types of parasomnias. In addition, other sleep disorders can manifest with a similar clinical presentation, for example, obstructive sleep apnea can lead to excessive movements and vocalizations caused by breathing difficulties [9]. Those who suffer from recurrent episodes of isolated sleep paralysis should be evaluated for excessive daytime sleepiness and cataplexy to rule out the diagnosis of narcolepsy. These occurrences should also be differentiated from nocturnal panic attacks and post-traumatic stress disorder [18]. Finally, parasomnias must be distinguished from nocturnal epilepsy attacks (sleep-related hypermotor epilepsy, SHE), which usually occur during slow wave sleep. Clinical presentation of seizures depends on the location of epileptogenic zone, yet signs such as stereotypical movements, dystonic or dyskinetic postures, and high speed and amplitude movements of the torso or limbs should raise physicians' suspicion. It is important to note that sleep disorders can be a provocative factor for epileptic seizures [24, 25]. Parasomnias can provoke epileptic seizures via mechanism of fragmented sleep or sleep deprivation [25]. In addition, sleep disorders are more prevalent in some epilepsy

Table 3. **Safety measures and sleep hygiene principles** [32]

Safety measures	Sleep hygiene
Sleeping alone or avoidance of direct physical contact with the partner (pillows or other physical barriers)	Avoiding large meals, alcohol, nicotine, blue light, caffeine, and active physical activity few hours before going to bed
Removal of hazardous/obstructing objects from the bedroom	Avoiding sleep deprivation
Sleeping on the lowest floor in the house	Maintaining a regular sleep–wake schedule with a constant waking time including weekends
Informing relatives, household members, and colleagues	Eliminating the use of alcohol and recreational drugs
Locking windows, balconies, and front door	Modification of work schedule (e.g., refusing shift work)
Front doors with entry and exit sensors with sound signal	Forming bedtime routine (quiet surroundings, dim lights, fresh air in the bedroom), application of meditation, relaxation techniques
Refrain from disturbing the person while experiencing parasomnias	
Lowering the height of the bed or mattress	
Removal of any weapons or dangerous household items	

patients. For example, NREM parasomnias are commonly reported by individuals suffering from sleep related hypermotor epilepsy, and their healthy family members indicating that impaired arousal control can play a role in pathophysiological mechanisms of both conditions [26]. Summarized clinical, diagnostic and differential diagnostic features of parasomnias are presented in Table 2.

MANAGEMENT

NREM sleep parasomnias

In accordance with NREM parasomnia phenotype and comorbidities, the standard therapy strategy includes ensuring safety of the patients and their family members, sleep hygiene (Table 3), modification of external and internal stimuli, management of comorbid conditions, and discontinuation or adjustment of the dose of prescribed medication that evoke abnormal sleep behaviours.

It is recommended to educate patients and their family members about priming and precipitating factors encouraging them to refrain from sleep deprivation, external stimuli, and emotional stress. As stated in a large cohort study of 512 participants, confining to sleep hygiene principles and ensuring the sleeper's safety resolved symptoms of 12.9% patients [7]. Consideration should be given to the management of other sleep disorders such as obstructive sleep apnea syndrome, restless leg syndrome, periodic limb movement and circadian sleep-wake rhythm disorders. According to a recent study, the management of comorbid conditions alone can resolve or diminish symptoms related to NREM parasomnias and should therefore be a first-line intervention prior to pharmacological treatment or psychotherapy [6]. There is efficient evidence that situational stress provokes NREM parasomnias and can be effectively reduced by cognitive behavioral therapy, whereas mindfulness exercises improve quality of sleep [7].

In case of inefficient non-pharmacological interventions, frequent abnormal behaviour episodes, sleep-related trauma, dangerous activities while sleeping or excessive daytime sleepiness, pharmacological treatment should be initiated. Except for sleep-related eating disorder, evidence supports clonazepam as a first-line therapy for NREM parasomnias [27]. If there are contraindications for prescribing benzodiazepines, it can be substituted with SSRI or tricyclic antidepressants. According to the large cohort study, clonazepam efficacy is 72.2%, while effectiveness of zolpidem, fluoxetine, citalopram, mirtazapine, melatonin range between 58–78% [7]. Different approach is applicable for sleep-related eating disorder since topiramate and sertraline were found to be efficacious in reducing night-time eating in patients with SRED [28]. Moreover, convincing evidence proves that circadian sleep-wake rhythm disorders could be cured with melatonin [11]. Psychotherapy should be recommended, if the patient refuses pharmacological treatment, experiences intolerable side effects, or claims that treatment is insufficient and expresses the need for psychological support.

REM sleep parasomnias

Patients with REM sleep parasomnias often have violent or unpleasant dreams, which provoke sudden, risky movements or shouting. Therefore, the first-line intervention should be ensuring safety in the bedroom by removing hazardous objects. Sleeping alone and confining to sleep hygiene principles is also beneficial (Table 3). Furthermore, alarm clock with motion sensor can detect sudden movements and gently awaken the patient, as awakening threshold tends to be low.

First-line pharmacological treatment is long-acting benzodiazepine clonazepam, although some side effects should be noted, such as daytime sleepiness, loss of equilibrium, falls, memory impairment, worsening of sleep-related breathing disorder [27]. Hence clonazepam should be prescribed with caution for patients with cognitive impairment, which are susceptible to falls or suffering from sleep apnea. It is crucial to foresee that sudden discontinuation of clonazepam could trigger recurrent or more frequent manifestation of REM sleep parasomnias. Melatonin could be recommended as an alternative, as side effects of this drug

are rare. According to a survey research, both melatonin and clonazepam were evaluated as equally effective, as they reduced intensity and frequency of REM parasomnias, although neither eliminated symptoms [29]. There is convincing evidence that increased muscle tone during REM sleep is associated with dopamine depletion [30]. Although, efficacy of dopamine agonist pramipexole remains disputable. Even though pramipexole effectively decreases severity of sleep-related symptoms, it only insignificantly improves symptoms for patients with comorbid Parkinson's disease. Dopamine agonists may provoke sleep fragmentation and insomnia, therefore arousing episodes of REM sleep parasomnias. Subsequently, dopamine agonists are not recommended for patients with Parkinson's disease. Standard strategy for the patient with comorbid Parkinson's disease includes modification of main antiparkinsonian medication by prescribing long-acting levodopa agent to be taken in the evening and/or avoiding dopamine agonists [31].

CASE No. 1

A 29-year-old male was examined due to suspected sleep disorder at the Department of Neurology of Lithuanian University of Health Sciences Kaunas Clinics. Complaints: nocturnal shouting, rearrangement of objects, sleepwalking, sometimes resulting in dressing up, leaving the house. The patient is also dissatisfied with the quality of sleep, often wakes up in the morning feeling unrested.

Case history: the patient has been experiencing parasomnias since childhood. Sleep disorders present once every night, according to relatives, during the first third of sleep. Similar behaviour is observed during daytime sleep. The patient has not had injuries during the episodes; however, he has once assaulted his mother. The patient regularly goes to sleep at around 11–12 p.m. and wakes up at around 6 a.m. Sometimes there are instances of longer sleep periods from 6 p.m. to 6 a.m. The patient's father and uncle from his mother's side have also experienced parasomnias. During 7-year period, the patient has been working shift work for several years, however the current job is also stressful. The patient's wife has noticed episodes of sleep apnea during his sleep. The patient has also had a nose septum fracture which was treated surgically; however, he's still experiencing chronic sinusitis symptoms. The patient's body mass is stable, without signs of obesity.

During objective and neurological clinical examination, no pathological symptoms were observed. Sleep questionnaires were used. Berlin sleep apnea questionnaire showed high risk of apnea. PADSS parasomnia severity evaluation scale: 15 points (pathological value). Innsbruck REM sleep behaviour disorders evaluation scale: 0.67 points (pathological value). No pathology was determined by Epworth sleepiness questionnaire, Insomnia severity index, Ullanlina narcolepsy, and Restless legs syndrome scales. Insomnia severity index and Ullanlina narcolepsy scales are adapted and validated for Lithuanian-speaking population, other scales are translated without adaptations.

Video polysomnography (Fig. 1 and Fig. 2): decreased sleep efficiency and dissociation between sleep stages were identified. REM sleep episode was registered at the beginning of sleep, although the patient had no symptoms indicative of narcolepsy. Therefore, the episode was evaluated as a consequence of chronic sleep deprivation. Most of the observed arousals were spontaneous, only few of them were related to the respiratory events, snoring, and movements. Combining video and polysomnography data, few episodes of parasomnias were registered: confusional arousal in N3 stage and talking and mumbling in N2 and N3 stages. No significant sleep-related breathing disorder was identified, AHI (apnea-hypopnea index) –

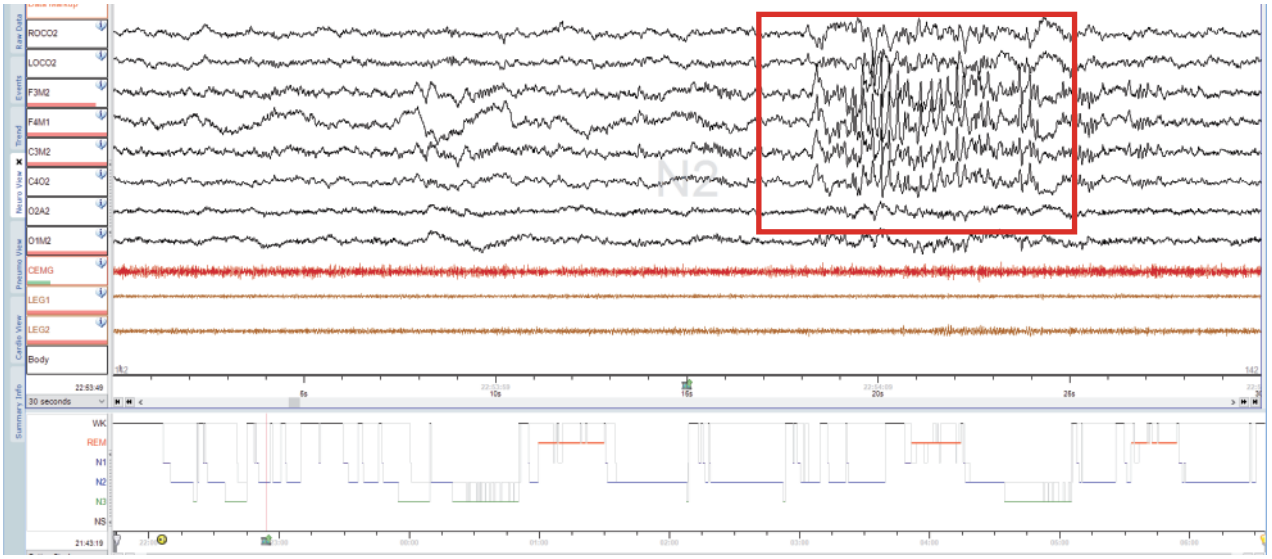

Fig. 1. **Instability of sleep stages indicative of NREM parasomnia.**
Hypersynchronous delta waves episode was registered during N2 stage, although it was replaced with regular N2 stage EEG activity after 7 seconds.

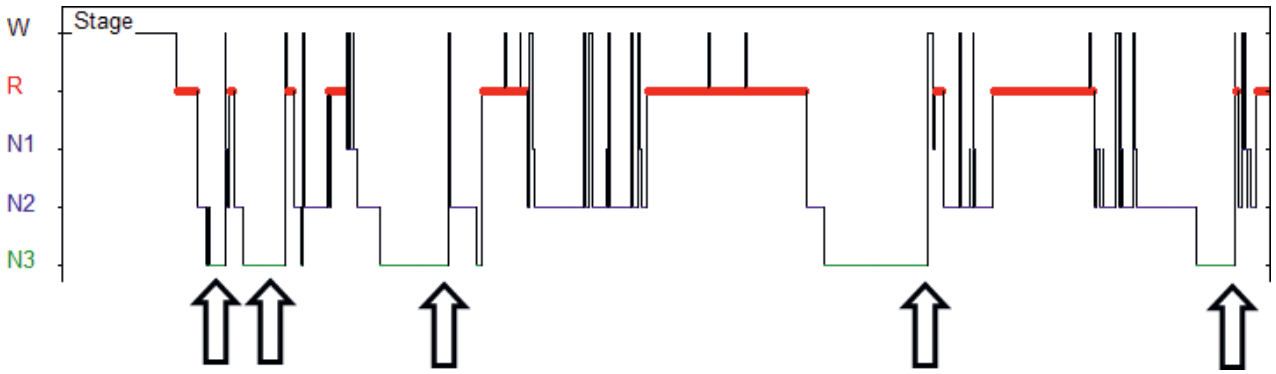

Fig. 2. **Hypnogram (structure of the patient's night sleep) of NREM parasomnia showing increased duration of N3 stage and sudden arousals from NREM sleep (marked with arrows)**

1.9/h, 14 episodes of hypopnea were registered, and total snoring time comprised 19.1% of sleep. Minimum SpO_2 was 91%, mean SpO_2 was 96%.

Clinical diagnosis: NREM parasomnia.

Recommendations and treatment: the patient was informed about precipitating factors, safety measures, and sleep hygiene principles. Melatonin (2–5 mg) was recommended to diminish the frequency and severity of parasomnias. In case of insufficient efficacy, paroxetine will be considered in the future.

CASE No. 2

A 56-year-old female was examined at the Department of Neurology of Lithuanian University of Health Sciences Kaunas Clinics. Complaints: the patient has been suffering from insomnia, as well as from episodes of active dream-enactment.

Case history: the patient has been suffering from episodes of insomnia for a long time. Inability to sleep has presented itself either as trouble falling asleep at the beginning of the night or as waking up too early. Previously, the patient was consulted by psychiatrists and prescribed fluoxetine and quetiapine for suspected generalized anxiety disorder. According to the patient, she started to experience active dream-enactment episodes while she was on the prescribed medications. During these occurrences she teaches lessons (the patient works as a teacher) or wanders around; she also complained of finding her door unlocked after one of these episodes. The patient has also hit her head against the wall while sleeping and called an ambulance, though she does not remember this episode. She was consulted by a neurologist, prescribed 1 mg of clonazepam, and discontinued fluoxetine and quetiapine. The number of sleep disturbances has decreased, but her sleep remains fragmentated, the patient wakes up at 3 or 4 a.m. and does not fall asleep anymore.

Neurological and physical examination: no pathological symptoms. Brain MRI: without pathological changes.

Video polysomnography (Fig. 3): good sleep efficiency and sleep architecture, normal sleep cycles. Ac-

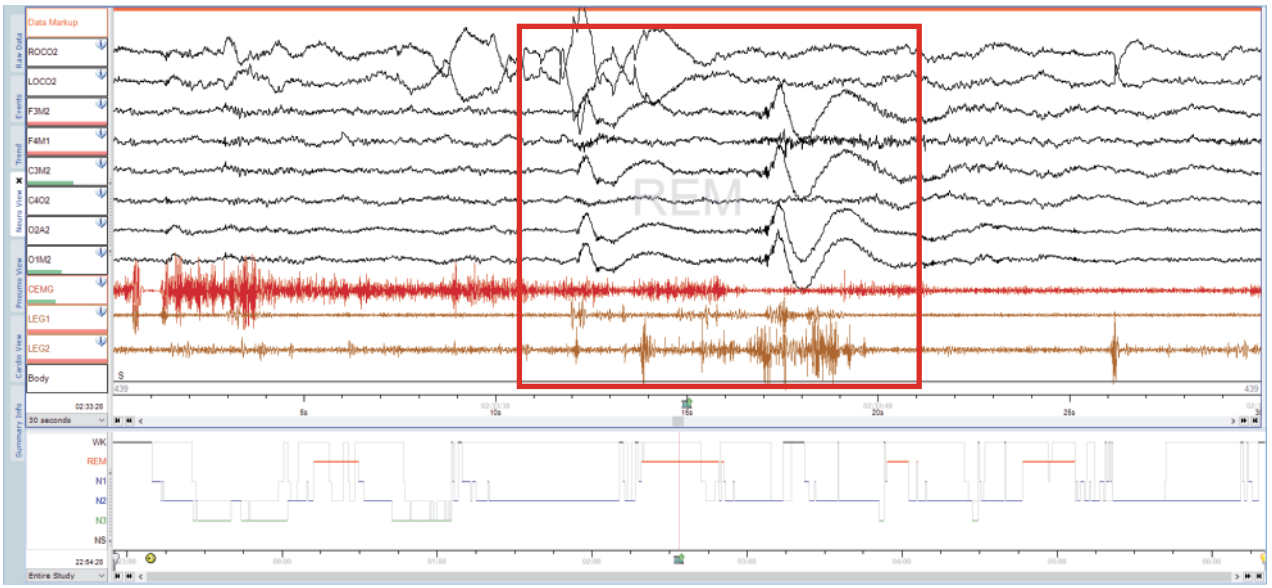

Fig 3. **Hypnogram of REM sleep behaviour disorder.**

During a 30-second episode of REM sleep, the chin (CEMG) and limbs (LEG1 and LEG2) electrodes registered muscle activity, which is not characteristic of the normal REM sleep hypnogram. The video showed that the patient was talking and moving her arms throughout the episode.

cording to SINBAR criteria, tonic REM sleep without atonia was registered in ~72% of tonic REM, and phasic RSWA – in ~50% of REM 3-second mini-epochs. In addition, motor and vocal activity was observed during REM stage: the patient talked, moved her arms, kicked with her legs, and tried to reach or place something in the air. Arousals were mostly spontaneous, a few were related to respiratory events, movement of limbs, and snoring. AHI (apnea-hypopnea index per hour of sleep) – 9.1/h, AHI in supine position – 9.1/h, and AHI on the left side – 8/h. 24 episodes of obstructive sleep apnea and 38 episodes of hypopnea were observed. Minimum SpO_2 was 82%, mean SpO_2 was 92%. Total snoring time comprised 32.5% of sleep. Periodic limb movement index was 24/h, periodic limb movement with arousals index was 2.3/h.

Clinical diagnosis: REM sleep behaviour disorder. Mild obstructive sleep apnea.

Treatment plan: 1) Avoidance of provoking actors and establishment of safe sleeping environment was suggested for the management of REM sleep behaviour disorder. Melatonin (3–5 mg) was prescribed and in case of insufficient efficacy, SNRI antidepressants (i.e., paroxetine) may be used. The patient should be re-evaluated by a neurologist, if the number of parasomnia episodes increases or other neurological symptoms begin to appear.

2) For the management of insomnia, it was recommended to continue cognitive behavioral therapy and avoid long-term use of benzodiazepines.

3) For the management of sleep apnea, it was recommended to maintain a healthy weight, avoid sleeping in supine position, and refrain from respiratory depressant medications (i. e. benzodiazepines).

4) The patient was informed about the possible risk of conversion to alpha-synucleinopathy in the future. Further neurological check-ups were scheduled.

CONCLUSION

NREM parasomnias is a family of sleep disturbances consisting of arousal disorders, which are divided into subtypes of confusional arousals, sleepwalking, and sleep terrors, as well as sleep-related eating disorder and sleep-related sexual behaviour disorder. REM parasomnias group includes REM sleep behaviour disorder, recurrent isolated sleep paralysis, and nightmare disorder. Clinical presentations of these sleep disturbances range from unpleasant experiences and minimal movements or mumbling during sleep to complex and sophisticated behaviours. One of the most important parts of the diagnostic process of parasomnias is obtaining a detailed anamnesis from the patient, his or her bed partner, and other witnesses of the episode. Additional testing, such as polysomnography, is often not necessary, although it is useful for differentiating between parasomnias or ruling out other sleep disorders, neurological and psychiatric pathologies. With the exception of RBD, as polysomnography is essential for its confirmation. Non-pharmacological interventions such as sleep hygiene and establishment of safe sleeping environment, as well as distinguishing and modifying priming and precipitating factors, play an important role in the management of parasomnias. If these measures fail, pharmacological treatment may be introduced.

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LĖTOJO IR PARADOKSINIO MIEGO PARASOMNIJOS: KLINIKINIAI ATVEJAI IR LITERATŪROS APŽVALGA

Santrauka

Parasomnijos – grupė miego sutrikimų, pasireiškiančių neįprastu elgesiu ar judesiais prieš užmiegant, miego metu ar prieš prabudimą. Pagal ICSD-3 (*International Classification of Sleep Disorders*) parasomnijos klasifikuojamos į lėtojo miego (NREM) ir paradoksinio miego (REM) parasomnijas. Lėtojo miego parasomnijoms priskiriami šie fenotipai: prabudimas su sumišimu, vaikščiojimas per miegus, naktinis siaubas, seksomnija ir su miegu susijęs valgymo sutrikimas. Lėtojo miego parasomnijos yra dažnesnės vaikams ir paaugliams bei yra gerybinis, savaime praeinantis arba nemedikamentinėmis priemonėmis koreguojamas susirgimas. Paradoksinio miego parasomnijoms yra priskiriami paradoksinio miego elgesio sutrikimas, miego paralyžius ir košmariški sapnai. Paradoksinio miego elgesio sutrikimas dažnesnis vyresnio amžiaus pacientams ir yra susijęs su neurodegeneracinėmis ligomis. Parasomnijos gali reikšmingai bloginti paciento ir jo partnerio gyvenimo bei miego kokybę, budrumą dieną, sukelti traumas. Detali miego anamnezė ir klinikinis ištyrimas turi itin svarbią reikšmę diferencinei diagnostikai tarp šių miego sutrikimų, taip pat naktinės epilepsijos priepuolių ir psichiatrinių ligų. Standartinė gydymo strategija apima bendruosius miego higienos principus ir miegančiojo bei aplinkinių saugumo užtikrinimą.

Raktažodžiai: miego sutrikimai, lėtojo miego parasomnijos, paradoksinio miego parasomnijos, polisomnografija.

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